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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,710	02/24/2004	Mark L. Nelson	PAZ-025CPCNRCE2	3651
959 7590 02/08/2008 LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER HAVLIN, ROBERT H	
			ART UNIT 1626	PAPER NUMBER
			MAIL DATE 02/08/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/786,710	Applicant(s) NELSON ET AL.	
	Examiner Robert Havlin	Art Unit 1626	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.138(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 30 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4,6-14,16,19,21,23-26,30-40,56-68,82 and 103-154 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,6-14,16,19,21,23,24,30-40,82 and 103-154 is/are rejected.
- 7) ☒ Claim(s) 25,26 and 56-68 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

**Status of the claims:** Claims 1-4, 6-14, 16, 19, 21, 23-26, 30-40, 56-68, 82 and 103-154 were pending in the application. Claims 1, 19, 21, 82, 149, 150 and 154 have been amended. Therefore, claims 1-4, 6-14, 16, 19, 21, 23-26, 30-40, 56-68, 82 and 103-154 are currently pending in the application.

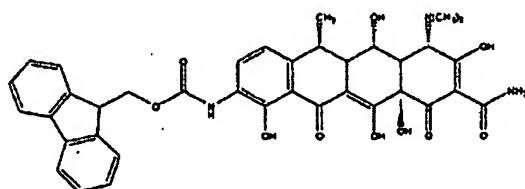
### *Double patenting*

The double patenting rejections of claims 1-4, 6-14, 16, 19, 21, 23, 24, 30-40, 82, and 140-154 are maintained.

### *Election / Restriction*

The elected group and species is cited from the office action of 1/5/2006:

Acknowledgement is made of Applicant's election (without traverse) of Group I  
and, for search purposes, the species,



, in a response filed 11/09/2005.

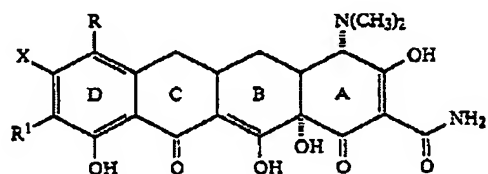
As detailed in the rejection below, no generic claim was found patentable; therefore, the claims are further restricted in scope to only the elected species. Subject matter reading outside the scope of the elected species is hereby withdrawn.

### *Claim Rejections - 35 USC § 102*

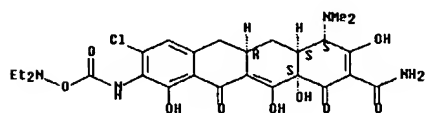
1. Claims 1-4, 6, 11-13, 16, 19, 21 and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Sum et al. (US 5,430,162).

Art Unit: 1626

2. The prior art reference teaches a genus of compounds of



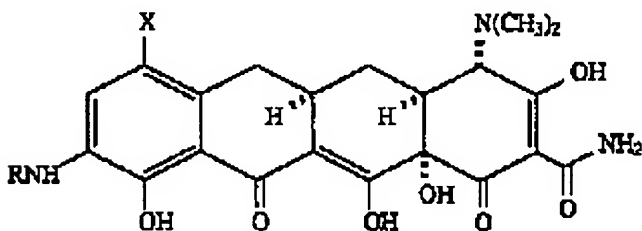
including the species of:



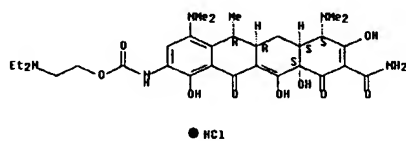
Here R9a of the instant claims is substituted alkylamino.

3. Claims 140-146, 148-150, and 154 are rejected under 35 U.S.C. 102(b) as being anticipated by Hlavka et al. (US 5,494,903).

Hlavka et al. teaches compounds of the formula



and the species of:



. Hlavka et al. reads on the instant claims where

R9a is substituted alkylamino.

**Claim Rejections - 35 USC § 103**

Claims 1-4, 11-13, 16, 18, 19, 82, 140-146, 148, and 154 were rejected under 35 USC 103(a).

Applicant eliminate the Markush alternatives "absent and prodrug," therefore overcoming the obviousness rejection, particularly in view of the restricted scope of examination.

***Claim Rejections - 35 USC § 112***

4. The rejection of claim 139 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's deletion of the term "substituted."

5. Claims 103-139 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Each of the claims alternatively claim a "prodrug ... thereof" form of the compounds described. The specification defines the term prodrug as:

Prodrugs are compounds which are converted in vivo to active forms (see, e.g., R. B. Silverman, 1992, "The Organic Chemistry of Drug Design and Drug Action", Academic Press, Chp. 8). Prodrugs can be used to alter the biodistribution (e.g., to allow compounds which would not typically enter the reactive site of the protease) or the pharmacokinetics for a particular compound. For example, a hydroxyl group, can be esterified, e.g., with a carboxylic acid group to yield an ester. When the ester is administered to a subject, the ester is cleaved, enzymatically or non-enzymatically, reductively or hydrolytically, to reveal the hydroxyl group.

[0237] The language "prodrug moiety" includes moieties which can be metabolized in vivo to yield an active compound. For example, the term includes moieties which can modify certain functional groups of the substituted tetracycline compounds, such as, but not limited to, hydroxyl groups and amino groups. In an embodiment, the prodrugs moieties are metabolized in vivo by esterases or by other mechanisms to hydroxyl groups, amino, amido or other groups which allow the substituted tetracycline compound to perform its intended function. Examples of prodrugs and their uses are well known in the art (See, e.g., Berge

Art Unit: 1626

et al. (1977) "Pharmaceutical Salts", J. Pharm. Sci. 66:1-19). Some prodrugs can be prepared in situ during the final isolation and purification of the compounds, or by separately reacting the purified compound in its free acid form or hydroxyl with a suitable esterifying agent. Hydroxyl groups, for example, can be converted into esters via treatment with a carboxylic acid (see, for example, Scheme 3). Examples of prodrug moieties include substituted and unsubstituted, branch or unbranched lower alkyl ester moieties, (e.g., propionic acid esters), lower alkenyl esters, di-lower alkyl-amino lower-alkyl esters (e.g., dimethylaminoethyl ester), acylamino lower alkyl esters (e.g., acetyloxymethyl ester), acyloxy lower alkyl esters (e.g., pivaloyloxymethyl ester), aryl esters (phenyl ester), aryl-lower alkyl esters (e.g., benzyl ester), substituted (e.g., with methyl, halo, or methoxy substituents) aryl and aryl-lower alkyl esters, amides, lower-alkyl amides, di-lower alkyl amides, and hydroxy amides. Preferred prodrug moieties for hydroxyl groups are propionic acid esters and acyl esters. Amino or amido groups can be modified by methods known in the art to form Schiff bases and other prodrugs which may or may not be metabolized in vivo.

which does not sufficiently convey to one skilled in the art what is being claimed. The definition incorporates a metabolic process which is entirely unknown. Furthermore, nothing in the claims themselves or in the specification indicates that the inventors had possession of the claimed "prodrug" form of the invention.

### ***Objections***

6. Claim 8, 113-116 are in improper dependent form.

### ***Conclusion***

No claim is in condition for allowance.

### ***Correspondence***

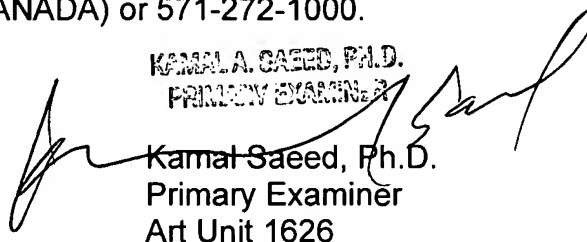
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Havlin whose telephone number is (571) 272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1626

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/  
Robert Havlin, Ph.D.  
Examiner  
Art Unit 1626

  
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